AMENDMENTS TO THE CLAIMS

Please CANCEL claims 124-138, 140, 142, 155-162, 164-168, 170, 172-175, 178-184, 202-216, 226-235 and 239, without prejudice.

Please AMEND the remaining claims and ADD new claims so that the claims read as follows:

124 - 138. (Cancelled)

139. (Currently Amended) A fusion protein adapted for passing across a cell membrane and incorporating an inhibitor moiety for inhibiting binding of a MAP kinase ~~with~~ to an integrin.

140. (Cancelled)

141. (Currently Amended) A fusion protein according to claim 139 further comprising a ~~carrier~~ facilitator moiety for facilitating passage across the cell membrane, wherein said facilitator moiety is linked to said inhibitor moiety.

142. (Cancelled)

143. (Currently Amended) An agent for inhibiting binding of a MAP kinase to an integrin, comprising:

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

a targeting moiety for targeting a cell expressing the integrin;

an inhibitor moiety for inhibiting binding of the MAP kinase ~~with~~ to the integrin; and

a ~~carrier~~ facilitator moiety for facilitating passage of the inhibitor moiety across the cell membrane of the cell, wherein said facilitator moiety is linked to said targeting moiety and said inhibitor moiety.

144. (Currently Amended) An agent according to claim 143, wherein the inhibitor and ~~carrier~~ facilitator moieties are capable of being released from the targeting moiety at the cell for passage of the ~~carrier~~ facilitator moiety and the inhibitor moiety across the cell membrane of the cell.

145. (Currently Amended) An agent according to claim 144, wherein the agent comprises an enzyme cleavage site for being cleaved to thereby release the ~~carrier~~ facilitator moiety and the inhibitor moiety at the cell.

146. (Currently Amended) An agent according to claim 145, wherein the enzyme cleavage site is a cleavage site for matrix-metalloproteinase-9 (MMP-9).

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

147. (Currently Amended) An agent according to claim 143 adapted for release of the inhibitor moiety from the ~~carrier~~ facilitator moiety after passage of the inhibitor moiety across the cell membrane of the cell.

148. (Previously Presented) An agent according to claim 143 wherein the targeting moiety is an antibody or a binding fragment of an antibody.

149. (Previously Presented) An agent according to claim 148, wherein the antibody or the binding fragment is specific for an extracellular region of the integrin.

150. (Currently Amended) An agent according to claim 143, wherein the targeting moiety is an integrin receptor targeted peptide ~~for binding~~that is capable of binding to the integrin.

151. (Currently Amended) An agent according to claim 143, wherein the inhibitor moiety is capable of binding to a binding site on the MAP kinase for the integrin or to the binding domain of the integrin for the MAP kinase.

152. (Currently Amended) An agent according to claim 151, wherein the inhibitor moiety comprises a binding domain of the integrin

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

for the MAP kinase or a ~~partial~~ core amino acid sequence of the binding domain that is capable of binding to the MAP kinase, or an analog or derivative thereof which is capable of binding ~~with~~ to the MAP kinase and thereby inhibiting binding of the MAP kinase to the integrin.

153. (Previously Presented) An agent according to claim 152, wherein the inhibitor moiety is an analog of the binding domain of an integrin subunit.

154. (Currently Amended) An agent for inhibiting binding of a MAP kinase to an integrin, comprising;

an inhibitor moiety for inhibiting binding of the MAP kinase to the integrin; and

a facilitator moiety for facilitating passage of the inhibitor moiety across the cell membrane of the cell, wherein said facilitator moiety is linked to said inhibitor moiety.

155 - 162. (Cancelled)

163. (Currently Amended) An isolated nucleic acid sequence encoding a fusion protein ~~as defined in claim 139~~adapted for passing across the outer cell membrane of a cell and incorporating an inhibitor moiety for inhibiting binding of a MAP

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

kinase to an integrin.

164 - 168. (Cancelled)

169. (Currently Amended) An expression vector incorporating a nucleic acid sequence as defined in claim 163 ~~for being expressed in a cell~~.

170. (Cancelled)

171. (Currently Amended) A host cell transformed with a vector as defined in claim ~~170~~169.

172 - 175. (Cancelled)

176. (Previously Presented) A pharmaceutical composition comprising a fusion protein as defined in claim 139 together with a pharmaceutically acceptable carrier or diluent.

177. (Currently Amended) A pharmaceutical composition comprising an agent for inhibiting binding of a MAP kinase with an integrin as defined in claim 143 or claim 154, together with a pharmaceutically acceptable carrier or diluent.

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

178 - 184. (Cancelled)

185. (Previously Presented) A method of screening for an agent capable of inhibiting binding of a MAP kinase to a binding domain of an integrin for the MAP kinase, comprising:

(b) determining if any said agent is capable of inhibiting binding of the MAP kinase to the binding domain of the integrin on the basis of the testing.

186. (Previously Presented) A method of screening for an agent capable of inhibiting binding of a MAP kinase to a binding domain of an integrin for the MAP kinase, comprising:

(a) testing a number of agents for ability to bind to either the MAP kinase or the integrin;

(b) selecting an agent or agents identified as being able to bind to the MAP kinase or the integrin on the basis of the testing; and

(c) utilising the selected said agent or agents in an assay for indicating whether the or any of the selected said agents is capable of inhibiting the binding of the MAP kinase to the binding domain of the integrin.

187. (Previously Presented) A method of evaluating whether an agent is capable of inhibiting binding of a MAP kinase to a

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

binding domain of an integrin for the MAP kinase, comprising:

(a) selecting the agent;

(b) utilising the agent in an assay for indicating whether the agent is capable of inhibiting the binding of the MAP kinase to the binding domain of the integrin; and

(c) determining if the agent is capable of inhibiting the binding of the MAP kinase to the binding domain of the integrin on the basis of the assay.

188. (Previously Presented) A method according to claim 187, wherein the integrin comprises $\beta 6$.

189. (Previously Presented) A method according to claim 187, wherein the MAP kinase is an ERK family member or a JNK family member.

190. (Previously Presented) A method according to claim 189, wherein the MAP kinase is ERK2.

191. (Previously Presented) An agent identified to be capable of binding to a binding domain of an integrin for a MAP kinase by a method as defined in claim 187.

192. (Previously Presented) An agent identified to be capable

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

of inhibiting binding of a MAP kinase to a binding domain of an integrin for the MAP kinase by a method as defined in claim 187.

193. (Currently Amended) A method ~~of~~ for isolating an agent from a sample utilising a molecule immobilised on a solid support and which agent is capable of binding to a binding site of a MAP kinase for an integrin, said method comprising comprising:

(a) contacting the molecule immobilised on the solid support with the sample under conditions suitable for binding of the agent to the molecule;

(b) eluting the agent~~,~~ from the solid support; and

(c) collecting the eluted agent.

194. (Previously Presented) A method according to claim 193, wherein the molecule is an integrin subunit of the integrin or an analog thereof.

195. (Previously Presented) A method according to claim 193, wherein the molecule is a fragment of an integrin subunit or an analog or derivative thereof.

196. (Currently Amended) A method according to claim 193, wherein the molecule is a polypeptide ~~as defined in claim 131~~ or an analog or derivative thereof.

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

197. (Currently Amended) A method according to claim 196, wherein the polypeptide comprises an amino acid sequence ~~RSKAKNPLYR~~selected from the group of sequences defined in SEQ ID NOS. 2, 3, 22 and 23.

198. (Previously Presented) A method according to claim 193, wherein the integrin comprises $\beta 6$.

199. (Previously Presented) A method according to claim 193, wherein the MAP kinase is an ERK family member or a JNK family member.

200. (Previously Presented) A method according to claim 199, wherein the MAP kinase is ERK2.

201. (Previously Presented) An agent isolated from a sample by a method as defined in claim 193.

202 - 216. (Cancelled)

217. (Currently Amended) A method ~~of~~ for modulating activity of a cell ~~expressing an integrin having a binding domain for a MAP kinase~~, the method comprising:

treating the cell with an effective amount of an agent ~~for~~

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

~~inhibiting~~that inhibits binding of ~~the~~ a MAP kinase to ~~the~~ a binding domain of ~~the~~ an integrin for said MAP kinase.

218. (Currently Amended) A method according to claim 217, wherein the agent ~~is a fragment as defined in claim 124~~comprises a fragment of said integrin comprising said binding domain or an analog or derivative thereof ~~capable of inhibiting~~that inhibits the binding of the MAP kinase to the binding domain of the integrin.

219. (Currently Amended) A method according to claim 217, wherein the agent ~~is~~ comprises a polypeptide ~~as defined in claim 131~~ or an analog or derivative thereof that ~~capable of inhibiting the binding of the MAP kinase with the binding domain of the integrin~~ inhibits the binding of the MAP kinase to the binding domain of the integrin.

220. (Currently Amended) A method according to claim 217, wherein the agent is a fusion protein ~~as defined in claim 139~~incorporating an inhibitor moiety that inhibits binding of the MAP kinase to the binding domain of the integrin.

221. (Currently Amended) A method according to claim 217, wherein the agent ~~is an agent as defined in claim 143~~comprises an

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

inhibitor moiety for inhibiting the binding of the MAP kinase to the integrin and a facilitator moiety for facilitating passage of the inhibitor moiety across the cell membrane of a cell, wherein the facilitator moiety is linked to the inhibitor moiety.

222. (Currently Amended) A method according to claim 217, wherein the agent binds to ~~is a peptide capable of binding with~~ the MAP kinase ~~to~~ and thereby inhibits binding of the MAP kinase to the binding domain of the integrin ~~for the MAP kinase~~.

223. (Previously Presented) A method according to claim 217, wherein the activity of the cell is growth of the cell.

224. (Previously Presented) A method according to claim 217, wherein the cell is a cancer cell.

225. (Currently Amended) A method according to claim ~~217~~ 224, wherein the cancer cell is a colon cancer cell.

226 - 235. (Cancelled)

236. (Previously Presented) A method according to claim 217 comprising administering to a mammal in need of such treatment an effective amount of the agent.

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

237. (Previously Presented) A method according to claim 236, wherein the method comprises therapy or prophylaxis of cancer or a condition associated with a predisposition to cancer.

238. (Previously Presented) A method according to claim 237, wherein the cancer is selected from the group consisting of cancer of the lip, tongue, salivary glands, gums, floor and other areas of the mouth, oropharynx, nasopharynx, hypopharynx and other oral cavities, oesophagus, stomach, small intestine, duodenum, colon, rectum, gallbladder, pancreas, larynx, trachea, bronchus, lung, breast, uterus, cervix, ovary, vagina, vulva, prostate, testes, penis, bladder, kidney, thyroid and skin.

239. (Cancelled)

240. (New) A method according to claim 222 wherein the agent binds to a binding site of the MAP kinase for the integrin.

241. (New) A method according to claim 217 wherein the MAP kinase is a member of the ERK family or the JNK family.

242. (New) A method according to claim 241 wherein the MAP kinase is ERK2.

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

243. (New) A method according to claim 217 wherein the integrin comprises an integrin subunit selected from β3, β5 and β6.

244. (New) A method according to claim 217 wherein the agent comprises a polypeptide having an amino acid sequence selected from the group consisting of RSKAKWQTGTNPLYR (SEQ ID No. 2), RARAKWDTANNPLYK (SEQ ID No. 22), RSRARYEMASNPLYR (SEQ ID No. 23), RSKAKNPLYR (SEQ ID No. 3), or an analog or derivative of the polypeptide which binds to a binding site of the MAP kinase for the integrin.

245. (New) A method according to claim 217 wherein the agent comprises a core amino acid sequence of the binding domain of the integrin, or an analog or derivative of the core amino acid sequence which binds to a binding site of the MAP kinase for the integrin.

246. (New) A method according to claim 217 wherein the cell is a cancer cell expressing the integrin selected from the group consisting of cancer cells of lip, tongue, salivary glands, gums, floor and other areas of the mouth, oropharynx, nasopharynx, hypopharynx and other oral cavities, oesophagus, stomach, small intestine, duodenum, colon, rectum, gallbladder, pancreas, larynx, trachea, bronchus, lung, breast, uterus, cervix, ovary,

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313

vagina, vulva, prostate, testes, penis, bladder, kidney, thyroid and skin.

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL (617) 542-2290
FAX (617) 451-0313